

SIMULATION OF THE DYNAMICS OF BIO-MEMBRANES IN A VISCOUS FLUID WITH A PHASEFIELD VARIATIONAL LAGRANGIAN APPROACH

C. Peco^{1*}, A. Rosolen¹ and M.Arroyo ¹

1: Laboratory of Computational Methods and Numerical Analysis. (LaCàN)
Universitat Politècnica de Catalunya
Campus Nord UPC, 08034 Barcelona, Spain
e-mail: christian.peco@upc.edu, web page: www-lacan.upc.edu

Key words: Bio-membranes, maximum-entropy, meshfree, Stokes, coupling, lagrangian, phase-field

Abstract. Bio-membranes are the basic separation structure in animal cells. Their complex behaviour, rich physical properties, formation and dynamics have been the object of experimental and theoretical investigation for biologists, chemists and physicists for many years. Bio-membranes are made out of several kinds of lipids self-assembled in a fluid bilayer, which presents a fluid behaviour in-plane and solid out-of-plane (curvature elasticity). Vesicles are closed fluid membranes, which play an important role in bio-physical processes such as transfer of proteins, antibodies or drug delivery into the cells. Vesicles serve as simplified models of more complex cell membranes, as well as the basis for bio-mimetic engineered systems. Bio-membranes only exist in solution and intimately interact with the surrounding fluid, which owing to the characteristic sizes and velocities, can be modeled with the incompressible Stokes equations. The aim of our work is to simulate the dynamics of the interaction between a bio-membrane and the fluid media surrounding. We take as basis our previous work on bio-membrane simulations [1], in which the solution of the fourth order PDE governing the bending elasticity of a vesicle is tackled with a phase-field or diffuse interface approach. The nonlinear, fourth-order PDE governing the phase field are conveniently solved using the local maximum-entropy (LME) approximants, a type of meshfree shape functions [2]. We merge the phase field model with the Stokes fluid media to treat naturally the coupling between the viscous forces in the fluid, the elastic forces due to the membrane, and the various constraints in the problem. The dynamics arise from a variational principle, and dictate the Lagrangian motion of the particles, convecting the phase field.

1 INTRODUCTION

Biomembranes or biological membranes have been object of experimental and theoretical investigation for biologists, chemists and physicists during many years. Biomembranes are composed by several kinds of lipids self-assembled in a fluid bilayer, which presents a liquid behaviour in-plane and solid out-of-plane. Vesicles are closed biomembranes which play an important role in biophysical processes and serve as simplified models of cell membranes to study aspects of the interaction between the lipid bilayer structure and the surrounding fluid. To simulate the dynamic behaviour of a vesicle both biomembrane solid structure and surrounding fluid have to be properly modelled. The Canham-Helfrich bending energy model is normally used to describe the solid behaviour, while the fluid is modelled as a Stokes flow. Two different approaches can be used to describe the equations for equilibrium shapes of vesicles in the continuum media approach, sharp-interface and phase-field or diffuse-interface models. In this work a phase-field model proposed by Du et al. [4] is used. This kind of models represent the interface between the inner and outer fluid as a diffuse-interface whose thickness is controlled by a transition parameter ϵ . The derived equations are highly non-linear and involve fourth-order spatial partial differential operators. The weak form of the equations necessitates piecewise smooth and globally C^1 continuous basis functions because products of second derivatives are involved in the integration of the variational formulation. The equations are discretized with LME [1] approximation schemes because they present interesting features such as positivity, monotonicity, variation diminishing property (the interpolation is not more wiggly than the data) and smoothness (C^∞). Adaptivity strategies are also required to make computationally affordable the phase-field approach. The fluid is commonly modelled as a Stokes flow because the Reynolds number is low. The idea is to apply the same numerical scheme to compute both the phase-field bending energy and the bulk effect of the fluid field surrounding the membrane. It is well-known that the Stokes problem lacks pressure stability if velocity and pressure are described with the same interpolation space, which demands a stabilization method to handle the problem. We borrowed finite element method (FEM) stabilization strategies to develop a LME stabilizing method. The structure of this paper is as follows. Section 2 introduces the formulation of the phase-field model and its numerical treatment. The capability of the adaptive strategy is also illustrated. In Section 3, we describe the Stokes flow problem and the stabilizing LME method, whose performance is tested through numerical benchmarks. Some concluding remarks are collected in Section 4.

2 MODEL OF THE BIOMEMBRANE: A PHASE-FIELD APPROACH

The phase-field model of a biomembrane is presented in this section. The numerical treatment, which includes discretization, nonlinear solver and adaptivity strategy, is also introduced. A numerical example of a dumbbell shape is set to evaluate the performance of the proposed scheme.

2.1 Problem formulation and numerical treatment

The phase-field model describing the equilibrium shapes for vesicles can be posed as an energy constrained-minimization problem:

Minimize

$$E(\phi) = f_E \frac{k}{2\epsilon} \int_{\Omega} \left[\epsilon \Delta \phi + \left(\frac{1}{\epsilon} \phi + C_0 \sqrt{2} \right) (1 - \phi^2) \right]^2 d\Omega \quad (1)$$

subject to

$$V(\phi) = \frac{1}{2} \left(Vol(\Omega) + \int_{\Omega} \phi d\Omega \right) = V_0 \quad (2)$$

$$A(\phi) = f_A \int_{\Omega} \left[\frac{\epsilon}{2} |\nabla \phi|^2 + \frac{1}{4\epsilon} (\phi^2 - 1)^2 \right] d\Omega = A_0 \quad (3)$$

where ϕ is the phase-field, ϵ the transition parameter, C_0 the spontaneous curvature, $f_E = \frac{3}{8\sqrt{2}}$, $f_A = \frac{3}{2\sqrt{2}}$, k the bending rigidity, V_0 and S_0 the volume and area constraints, respectively.

These equations are discretized with LME approximation schemes, augmented Lagrangian methods are used to impose the linear and nonlinear constraints, while L-BFGS and Newton-Rahpson techniques are applied to solve the nonlinear problem. An adaptive algorithm based on Centroidal Voronoi Tessellations [5] is proposed to reduce the computational cost. A detailed explanation about the approximants, the discretization procedure, the numerical strategy to solve the problem and the adaptive algorithm is given in [6].

2.2 Numerical example

The energies computed for the dumbbell equilibrium shape considering different values of ϵ and several levels of refinement for uniform grid of points can be seen in Table 1. The number of nodes for each grid and the values of the average nodal spacing \bar{h} (average element size in FEM terminology) are denoted in the first and second column, respectively. The remaining columns correspond to the values of energies for different values of transition parameter ϵ .

It is remarkable that the accuracy of phase-field results is intrinsically associated to the value of the transition parameter ϵ , which is in turn directly related with the size of the discretization: we consider that the relation $\epsilon \geq 2h$ is quite reasonable. In Table 1 it is shown that values of energy converge for each fixed ϵ (columns) and the error becomes gradually less as the grid of points is refined. The largest errors are presented by the values of the upper supra-diagonal, and it happens because they do not fulfill the mentioned relation between the transition parameter and the discretization size.

The effect of the adaptive strategy applied to a grid of 6124 points is shown in Figures 1 and 2, respectively. Former illustrates the grid of points, while latter the phase-field

# nodes	\bar{h}	$\epsilon = 0.05$	$\epsilon = 0.04$	$\epsilon = 0.03$	$\epsilon = 0.02$	$\epsilon = 0.01$
6124	0.024	9.29504	9.15560	–	–	–
12271	0.017	9.30167	9.15918	9.00361	–	–
24597	0.012	9.30627	9.16106	9.00310	8.87045	–
49145	0.0084	9.31053	9.16315	9.00362	8.86669	–
98388	0.0059	9.31307	9.16407	9.00331	8.86445	8.81432
146545	0.0048	9.31439	9.16421	9.00217	8.86005	8.77677
296344	0.0034	9.31650	9.16512	9.00251	8.86033	8.77359

Table 1: Energies of the dumbbell equilibrium shape for different uniform grids of points and several values of ϵ .

solutions. The value of the transition parameter ϵ , and thus the value of the average nodal spacing \bar{h} , is decreased in each step. The accuracy obtained at the end of the process reaches that obtained with a uniform grid of 296344 points.

The effect of the adaptive strategy applied to a grid of 6124 points is shown in Figures 1 and 2, respectively. Former illustrates the grid of points, while latter the phase-field solutions. The value of the transition parameter ϵ , and thus the value of the average nodal spacing \bar{h} , is decreased in each step. The accuracy obtained at the end of the process reaches that obtained with a uniform grid of 296344 points.

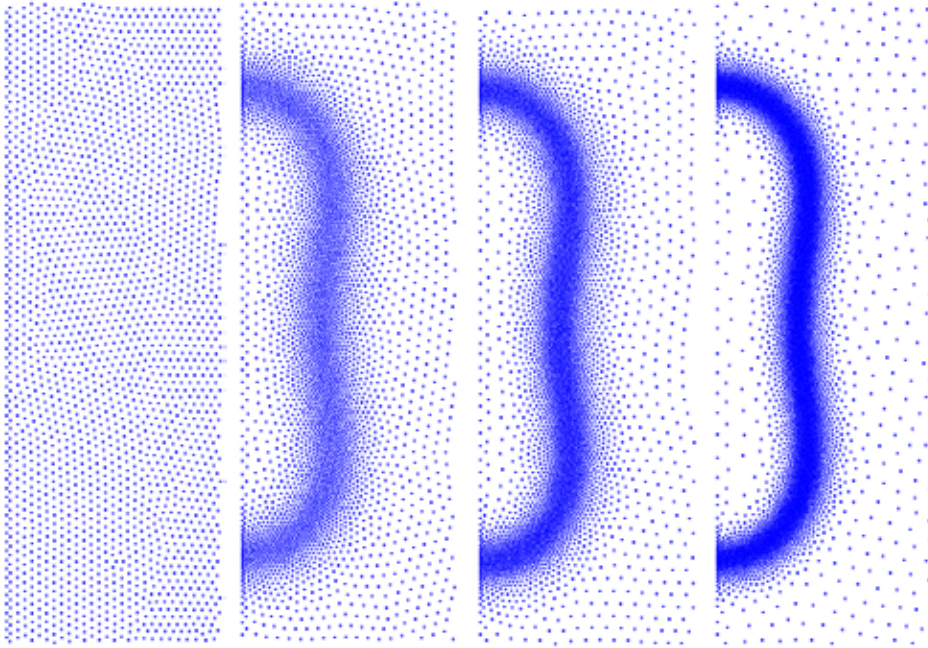


Figure 1: Adapted grid of 6124 points corresponding to the dumbbell equilibrium shape. The average nodal spacing \bar{h} decreases from left to right.

Three-dimensional views of the dumbbell equilibrium shape are illustrated in Figure 3.

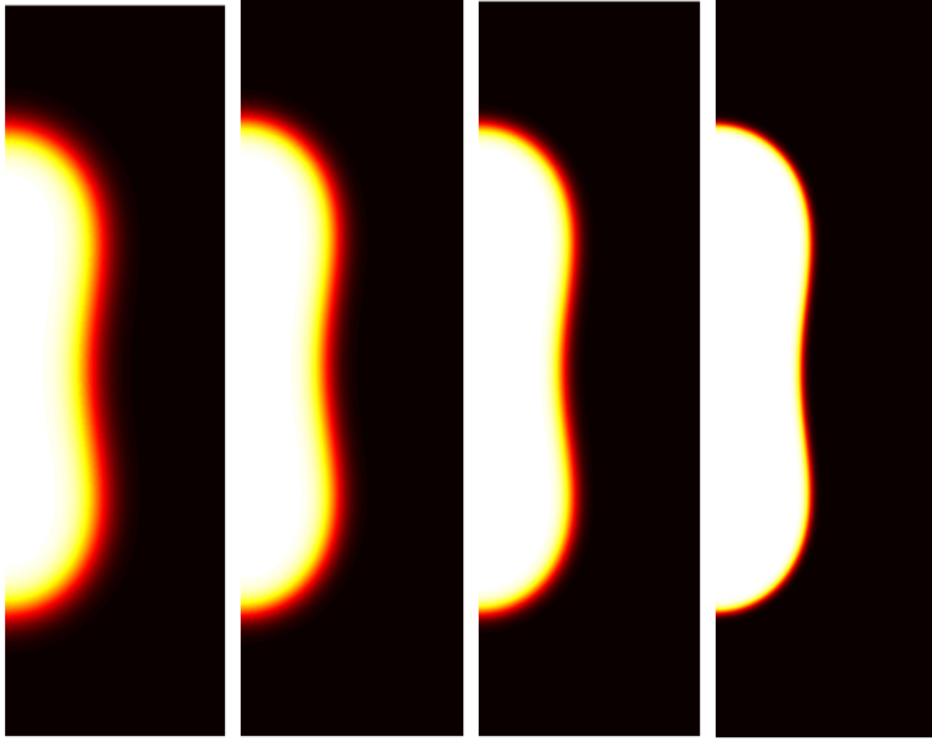


Figure 2: Phase-field density for different grids of 6124 points corresponding to the dumbbell equilibrium shape.

3 MODEL OF THE FLUID: STOKES FLOW

The Stokes flow problem and the stabilization with LME approximation schemes are explained in this section. The performance of the method is illustrated with classical benchmark tests.

3.1 Introduction

The Stokes problem can be formulated in general form as:

$$-\nu \Delta u + \nabla p = f \quad \text{in } \Omega \quad \nabla \cdot u = 0 \quad \text{in } \Omega \quad u = u_d \quad \text{on } \Gamma_d \quad (4)$$

where v is the velocity, p the pressure, f the vector of body forces, ν the kinematic viscosity, and $\Omega \subset \mathbb{R}^d$.

Let be $V = H_0^1(\Omega)^d$ and $Q = L_2(\Omega)/\mathbb{R}$ the velocity and pressure spaces, respectively. Then, the weak form is set to find $u \in V$ and $p \in Q$ such that:

$$a(u, v) - b(p, v) = l(v) \quad v \in V \quad b(q, u) = 0 \quad q \in Q \quad (5)$$

This weak form is widely studied in literature, and it is well-known that the existence and uniqueness of the solution require equations to satisfy the Ladyzhenskaya-Babuška-

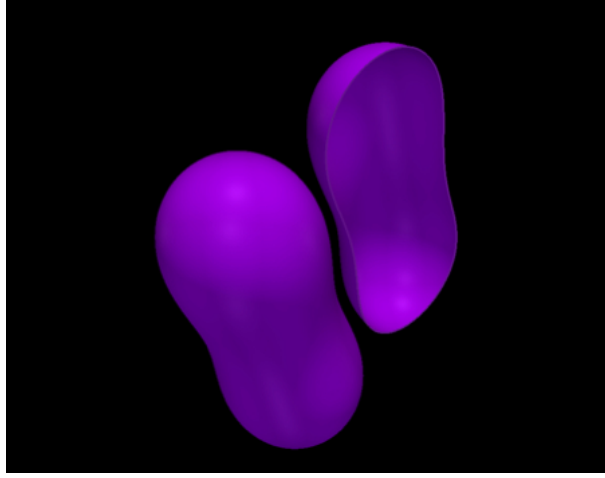


Figure 3: 3D view of the dumbbell equilibrium shape.

Brezzi (LBB) condition. This rule states that the following inf-sup condition has to be fulfilled to guarantee the stability of the system (matrix of the system derived non singular):

$$\inf_{q \in Q} \sup_{v \in V} \frac{b(q, v)}{\|q\|_Q \|v\|_V} \geq K_b > 0 \quad (6)$$

This condition holds true if $b(q, v) = (q, \nabla \cdot v)$, $q \in Q = L_2(\Omega)/R$ and $v \in V = H_0^1(\Omega)^d$, properties which are always kept by the Stokes problem at a continuous level. Unfortunately, when the equations are discretized with restrictive spaces, that is, $Q_h \subset Q$ and $V_h \subset V$, the LBB condition can fail and the pressure become unbounded. In particular, it is proven that using the same discretization space for both pressure and velocity results in a loss of stability, which is the cardinal issue of numerical methods for solving the Stokes problem.

3.2 Stabilization of Stokes equations

Main strategies to deal with this obstacle are mixed formulations and stabilization of Stokes equations. The mixed formulations tackle the problem by seeking admissible pairs of spaces that fulfill the inf-sup condition. Stabilization techniques use a discretization based on a single space for both pressure and velocity, and add terms to the original weak form to give coercivity to the resulting matrix.

We are interested in the coupled problem posed by the bending model of biomembranes and the Stokes flow in which they are immersed. LME approximants present nice characteristics to solve the phase-field governing the structure behaviour and, to earn simplicity in the numerical scheme and reduce the computational cost, we find convenient to use the same discretization space for the fluid problem.

Stabilization techniques have undergone a large and satisfactory development in the FEM context [3]. We develop a LME stabilization method inspired in FEM stabilization ideas. Because of the noticeable differences between FEM and LME, the application of the FEM based methods is not direct and redefinition of parameters is needed. The discretization of the Stokes problem leads to the following system:

$$\begin{bmatrix} K & -D^T \\ D & 0 \end{bmatrix} \begin{bmatrix} U \\ P \end{bmatrix} = \begin{bmatrix} F \\ 0 \end{bmatrix} \quad (7)$$

where K comes from the Laplacian velocity and it is definite positive, while D corresponds to the pressure terms and introduces the instability to the total matrix. To stabilize the system we need to add an extra term to the weak form [3]:

$$\int_{\Omega} \tau \mathcal{P}(w, q) \mathcal{R}(u, p) d\Omega \quad (8)$$

where $\mathcal{R}(u, p)$ is the residual or strong form of the problem (which ensures the consistency of the new weak form), τ is a parameter which controls the measure of the stabilization to be applied and \mathcal{P} is a partition of the differential operator. Different choices of this partition lead to different stabilization methods.

To summarize the effect of the stabilization methods and to provide an integrated way of implementation in the code, the following general term becomes adequate from now on [2]:

$$\int_{\Omega} \tau_1 (-\alpha \nu \Delta w + \beta_1 \nabla q) (-\nu \Delta u + \nabla p - f) d\Omega \quad (9)$$

where α and β_1 are parameters that take values 1, 0, -1 the former, and 1, -1 the latter. The different combinations of the values enable the user to jump from one stabilization method to another while maintaining the same term structure.

This last expression can be developed in a larger group of terms to add their discretized matrices to the original matrix form of the Stokes problem, resulting:

$$\begin{bmatrix} K + \alpha K_{st} & -D^T - \alpha D_{st}^T \\ \beta_2 D - \beta_1 D_{st} & \beta_1 L_{st} \end{bmatrix} \begin{bmatrix} U \\ P \end{bmatrix} = \begin{bmatrix} F - \alpha F_{st}' \\ \beta_1 F_{st}'' \end{bmatrix} \quad (10)$$

where $\beta_2 = -\beta_1$ and L_{st} is a positive definite matrix since comes from a pressure Laplacian. This matrix gives to the global matrix the stabilization needed to be non singular and subsequently provide a solution for the system.

The parameter τ is a stabilization parameter that have to be defined by the the method, an which usually involves a constant to be calibrated by the user. In FEM, some expressions that work element wise have been developed, performing very well. Since in LME we work with a set of points instead of a mesh, some redefinition of the parameter has to be worked out. In FEM, the normal parameter to use is the nodal spacing. In meshless methods, this nodal spacing is usually interpreted as a the range of the shape functions,

creating functions-wise parameters. Here we propose an expression based on this concept but defining a pointwise parameter, which show a fairly direct way for implementation and excellent results in simulations.

$$\tau_1 = \frac{C}{\nu} \bar{\rho}^2; \quad (11)$$

where $\bar{\rho}$ is the mean over the neighbors, $N\bar{\rho} = \sum_{i=1}^N \rho_i$ with $1, 2, \dots, N$ the list of neighbors of gauss point.

3.3 Numerical examples

We select and apply the GLS-LME stabilization technique ($\alpha = 1$ and $\beta_1 = 1$) to the classical Poiseuille and Colliding flows benchmark tests for the Stokes problem. Here we only illustrate the performance of the method for the Colliding flow, but similar results were obtained for the Poiseuille problem. Since these tests have analytical solution we can accurately compare the results of the simulations.

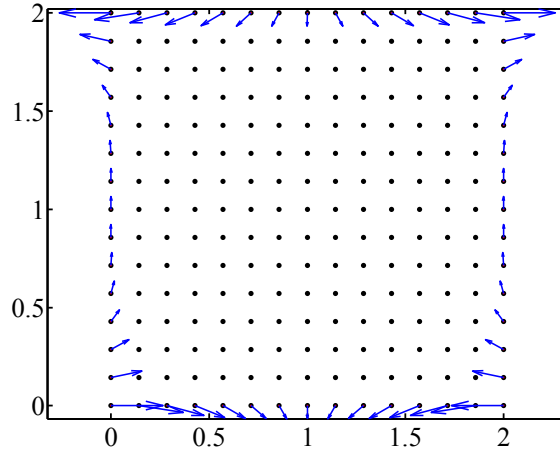


Figure 4: Definition of the Colliding flow problem.

The essential boundary conditions of the problem are plotted in Figure 4. The velocity field is illustrated in the Figure 5 without the application of stabilizing method (left) and after stabilization (right). Although we have illustrated the solutions corresponding to a coarse grid of points for clearness purposes, the observed patterns are maintained in refined grids. The velocity stabilized solutions do not present a strange physical behaviour when compared with the analytical one. The same behaviour can be seen in the Figure 6 where we plot the pressure for the solution without stabilization. Disproportionate values of pressure and oscillations are observed. This anomalous behaviour disappears after the

stabilization and the obtained solution recovers the smoothness, matching the analytical field.

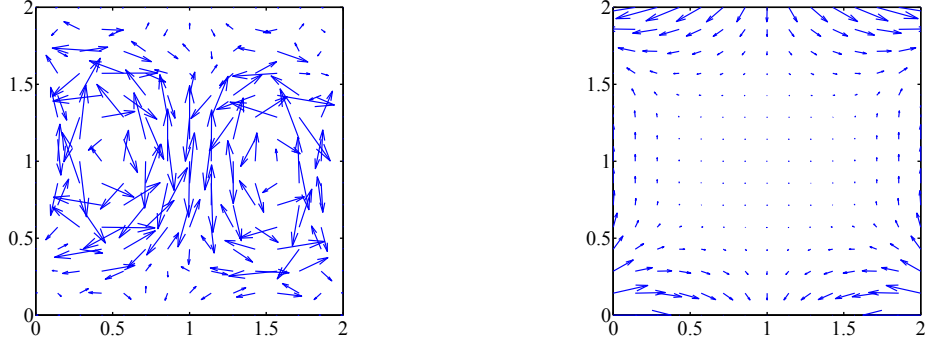


Figure 5: Colliding flow velocity stabilization: (left) Velocity field with no stabilization computed with 225 nodes, and (right) Velocity field stabilized computed with GLS-LME, 225 nodes and $\gamma = 1.0$.

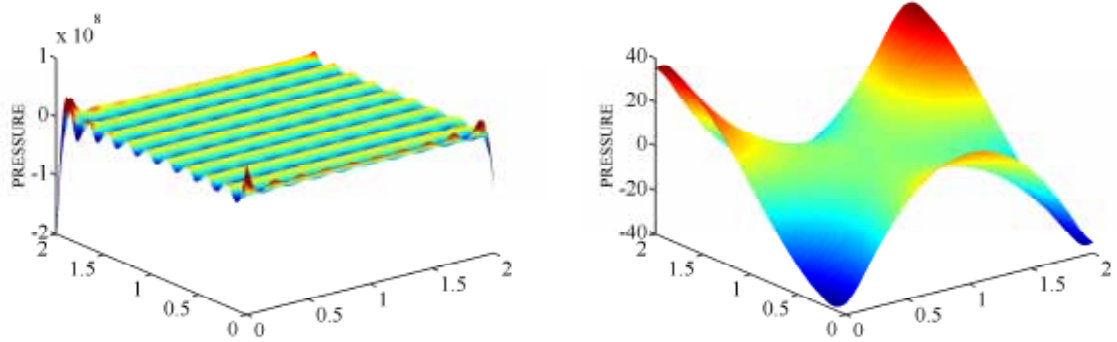


Figure 6: Colliding flow pressure stabilization: (left) Pressure field with no stabilization computed with 625 nodes, and (right) Pressure field stabilized computed with GLS-LME, 625 nodes and $\gamma = 1.0$.

This fact is reflected in detail with the recovery of the optimal rate after the stabilization in the convergence charts for L_2 norm, as it is illustrated in the Figure 7.

Another set of simulations have been run over an unstructured grid in order to test the capability of the point-wise τ_C parameter introduced before. As can be observed in 7, both for pressure and velocity the optimal slopes are recovered. This important result enables the use of this fairly direct implementation parameter to manage adaptive processes which are needed in high accurate or tridimensional computations.

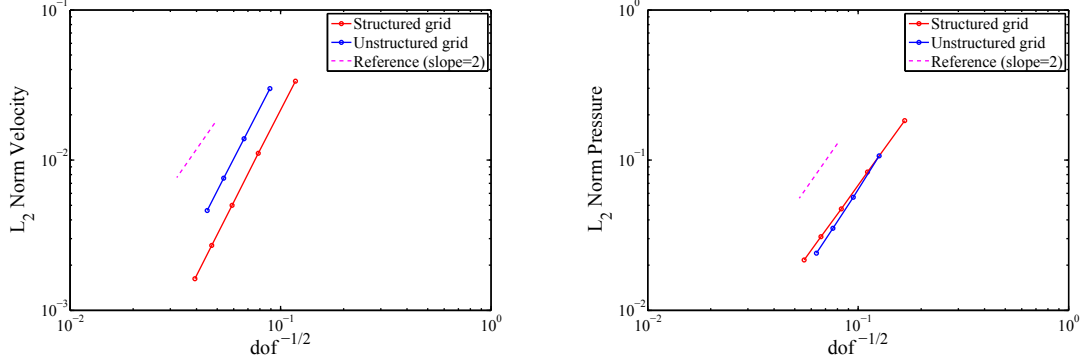


Figure 7: Colliding flow velocity stabilization: (left) Velocity field with no stabilization computed with 225 nodes, and (right) Velocity field stabilized computed with GLS-LME, 225 nodes and $\gamma = 1.0$.

4 COUPLING STRATEGY AND NUMERICAL EXAMPLES

Once the main two ingredients of the numerical simulation have been tested and performed separately, a coupling strategy have to be set in order to generate an efficient algorithm which can represent the evolution of a biological process. The idea we present here is a change of scope from a phase-field eulerian approach to a fully lagrangian one where the phase-field no longer will be solved over a stationary set of points, but will be considered as a material property which is transported within the fluid and therefore solved in terms of its final position. This immediately generates a coupled monolithic algorithm where the Stokes equations are solved considering the potential forces coming from the phase-field bio-membrane.

We state the dynamic problem from a variational standpoint (stokes) by setting an optimization over the total system incremental energy \dot{W} (biomembrane bending energy change and Stokes bulk fluid dissipation)

$$\dot{W} = \dot{E} + D \quad (12)$$

Being E the bending elastic energy of the biomembrane in terms of a phase-field ϕ , and D the dissipation, which become described as:

$$E = \frac{k}{2\epsilon} \int_{\Omega_t} (\epsilon \Delta_t \phi_t + (\frac{1}{\epsilon} \phi_t + c_0 \sqrt{2})(1 - \phi_t^2))^2 d\Omega_t \quad (13)$$

$$D = \int_{\Omega_t} 2\mu \Delta : \Delta + \kappa (\nabla \cdot v)^2 d\Omega_t \quad (14)$$

Where $\Delta = \frac{1}{2}(\nabla v + \nabla v^T) - \frac{1}{3}I(\nabla \cdot v)$ and Ω_t the space domain at time t .

This expression can be worked out taking into account the incompressibility of the media, leading to the following simplified expression

$$\mathcal{D} = \int_{\Omega_t} \mu |\nabla v|^2 d\Omega_t \quad (15)$$

Which will be used from now on as the dissipation expression for the bulk Stokes fluid.

We discretize the original time interval for a process in smaller time steps $[t_0..t_k, t_{k+1}..t_{end}]$, and calculate the evolution between two generic states t_k and t_{k+1} , by applying a minimization over the incremental energy,

$$\Delta \mathcal{E}_{k \rightarrow k+1} = \int_{t_k}^{t_{k+1}} W dt \approx W_{k \rightarrow k+1} \Delta t \quad (16)$$

We define,

$$W_{k \rightarrow k+1} = \dot{E}_{k \rightarrow k+1} + \mathcal{D}_{k \rightarrow k+1} \quad (17)$$

The differential equation is

$$\partial_\varphi \partial_t E(\varphi, \varphi_t) + \partial_\varphi \dot{D}(\varphi_t) = 0 \quad (18)$$

If we use a classic alpha-method to integrate through time, we have

$$W_{k \rightarrow k+1} = \theta \dot{W}_{k+1} + (1 - \theta) \dot{W}_k \quad (19)$$

The aim of the algorithm is to minimize the whole energy action at a given step, setting all the expressions in terms of an unknown deformation mapping. The calculations will be brought to the reference state, in which the spatial discretization will take place, by means of mesh-free shape functions. A numerical simulation over an axisymmetric cilinder with a bio-membrane embedded can be observed in figure 8, where the forces of the elastic potential coming from the phase-field can be seen over the fluid domain, governing the evolution for the shape, which can be identified following the line where forces are stronger.

5 CONCLUSIONS

We explain how the biomembranes structural behaviour can be modeled through an energy constrained-minimization phase-field problem. We indicate algorithms to solve the problem and also propose an adaptive strategy based on LME approximants and Centroidal Voronoi Tessellations. We illustrate the performance of the proposed method with a representative example of a dumbbell equilibrium shape.

We propose a stabilization technique inspired in the well-known FEM stabilization methods to solve the Stokes problem with LME. We design a pointwise stabilization parameter suitable for the new environment and we illustrate the capability of the proposed scheme in the classical Colliding flow benchmark problem.

We present a coupling algorithm based on a lagrangian variational approach which enable us to represent the dynamics of an evolution by means of a monolithic scheme, using the deformation mapping to solve both the membrane and the fluid.

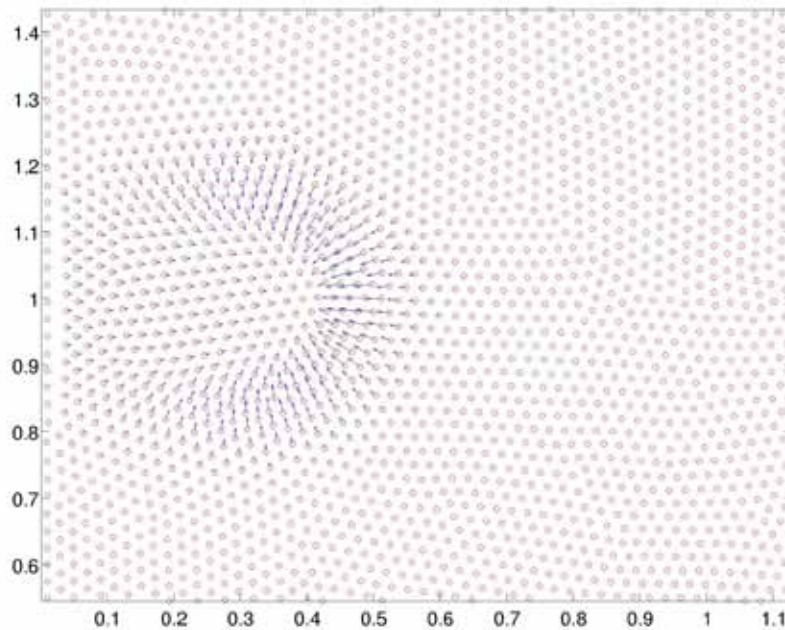


Figure 8: Elastic forces over fluid domain of 6124 nodes and $\gamma = 0.8$.

REFERENCES

- [1] M. Arroyo and M. Ortiz, *Local maximum-entropy approximation schemes: a seamless bridge between finite elements and meshfree methods*, International Journal for Numerical Methods in Engineering **65** (2006), no. 13, 2167–2202.
- [2] T. Barth, P. Bochev, M. Gunzburger, and J. Shadid, *A taxonomy of consistently stabilized finite element methods for stokes problem*, Siam Journal on Scientific Computing **25** (2004), 1585–1607.
- [3] R. Codina, *Comparison of some finite element methods for solving the diffusion-convection-reaction equation*, Computer Methods in Applied Mechanics and Engineering **156** (1998), 185–210.
- [4] Q. Du, C. Liu, and X. Wang, *A phase field approach in the numerical study of the elastic bending energy for vesicle membranes*, Journal of Computational Physics **198** (2004), 450–468.
- [5] Q. Du, V. Faber, and M. Gunzburger, *Centroidal Voronoi Tessellations: Applications and Algorithms*, SIAM Review **41** (1999), no. 4, 637–676.

- [6] A. Rosolen and C. Peco and M. Arroyo, *An adaptive maximum-entropy meshfree method for phase-field models of axisymmetric biomembranes*, To be submitted to Journal of Computational Physics (2011).